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Beyond Ebola: lessons to mitigate future pandemics



It is now just more than a year since the official confirmation of an outbreak of Ebola haemorrhagic fever in west Africa.¹ With new cases occurring at their lowest rate for 2015,² and the end of the outbreak in sight for all three countries predominantly affected, now is the time to consider strategies to prevent future outbreaks of this, and other, zoonotic pathogens. The Ebola outbreak, like many other emerging diseases, illustrates the crucial role of the ecological, social, political, and economic context within which diseases emerge. Increasing anthropogenic environmental changes, coupled with a globalised network of travel and trade, allow zoonotic pathogens to spill over into human beings with increasing frequency, and leave us supremely vulnerable to their international spread.³ Pandemics are no longer simply the domain of public health and clinical medicine, but are a social issue, a development issue, and a global security issue.

The cost of management of infectious disease outbreaks is almost always greater than the cost of avoiding them. For severe acute respiratory syndrome (SARS), the global cost of a single outbreak was estimated to be between US\$13 billion and US\$50 billion at the currency values of the 2003 outbreak.^{4,5} For Ebola, the cost might be higher—both in the direct, short-term cost of control, patient care, and hospital admission, and in the indirect, longer-term dislocation of the regional economies in west Africa.⁶ The economic costs of disease emergence are projected to continue to rise in line with increasing frequency of outbreaks driven by expanding socioeconomic and environmental changes that cause diseases to emerge.⁷ Mitigation of future pandemic threats such as Ebola is therefore more cost-effective than the current approach of responding to outbreaks after they have begun to spread rapidly in the human population.⁷

What would mitigation strategies to deal with future pandemic risks of zoonotic disease look like? Analyses of emerging disease trends during the past six decades have shown that Ebola fits the dominant pattern.⁸ This pattern involves zoonotic spillover from wildlife or livestock driven by changes in land use, crop choices, migration patterns, animal husbandry, trade, transport, and travel.⁹ The west African Ebola outbreak, similar to previous outbreaks of Ebola, HIV, SARS, influenza, and most other emerging diseases, probably began with a zoonotic

spillover from a wildlife reservoir, in this case thought to be bats.¹⁰ Targeted programmes for behaviour change, focusing on incentives for bushmeat hunting, should be part of the mitigation strategy. This approach was trialled in central Africa, with education programmes designed to reduce the consumption of primates found dead in forests, and has been shown to offer a cost-effective way to mitigate the risk of an Ebola outbreak.¹¹ Additionally, projects aimed to reduce dependency on bushmeat need to be supported, either through creative approaches to farming of some wildlife species, or by expansion of livestock production, with appropriate biosecurity and surveillance to prevent emergence of other zoonoses.

The acceleration of vaccine development for Ebola as part of an outbreak control strategy could also have a crucial role to mitigate future outbreaks. Ebola's propensity for nosocomial spread (noted in west Africa and in many previous Ebola outbreaks) could be curtailed by preoutbreak vaccination of critical care workers in Ebola virus hotspots. Likewise, targeted training in infection control, and efforts to maintain surge capacity between outbreaks, will be crucial for rapid response to the first cases in a future emergence event.

Can these approaches be scaled up to mitigate future pandemics on a global scale? Global mitigation of future pandemic risk must focus on the large-scale behaviours that lead to zoonotic spillovers. This approach means engaging with the sectors that drive disease emergence, including industries involved in land-use change, resource extraction, livestock production, travel, and trade, among others. Large economic development programmes will need health-impact assessments that deal explicitly with the risk of emergence of novel diseases, and plans to set up new clinics and surveillance programmes listed as project deliverables. An improved understanding of the liability for disease emergence will drive this change; when all are at risk, collective action is needed to strengthen the weakest links in the chain.^{12,13} Although existing multilateral agreements (eg, the International Health Regulations) allow for some coordination of national responses to outbreaks and bilateral interventions to build public health capacity in poor countries, more is needed. Collective investment needs to occur through a mechanism similar to the Global Environment Facility,

not just in local public health infrastructure, but also in so-called one health measures to reduce the likelihood of zoonotic spillovers. Management of future risk will need anticipation of the origin and spread of diseases through improved predictive models of emergence that include animal populations, the powerful new drivers of global trade and travel, and the effect of disparities in income and wealth on health infrastructure, risk mitigation, presymptomatic diagnosis, and vaccination.^{14,15}

Perhaps the biggest challenge is that the identity of future emerging diseases will often be unknown before emergence (eg, as in SARS and HIV). Is it possible to design a strategy for an as-yet unknown pathogen? This task seems daunting, but it has already begun, partly through reduction of the size of the problem and allocation of resources in an objective way to the locations most at risk. Analysis of trends in disease emergence provides a strategy to identify the places most likely to propagate the next pandemic.³ These hotspots for disease emergence tend to be tropical regions with high wildlife diversity that harbour known or unknown zoonoses, and high levels of socioeconomic and environmental change.³ USAID's Emerging Pandemic Threats (PREDICT) programme targets these hotspots to identify known and previously unknown viruses in wildlife species known to be zoonotic reservoirs, analyses patterns of high-risk human behaviour, tests people for evidence of these viruses moving across the species barrier, and enables the design of strategies to reduce the risk of even the first spillover event.⁸ Identification of the next Ebola virus, or the next HIV, will not be a simple task, but estimates of the diversity of viruses existing on the planet show that it is not impossible.¹⁶ Surely this threat is worth concerted effort, given the human tragedy and economic devastation when pandemics strike.

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- 1 WHO Regional Office for Africa. Ebola virus disease in Guinea. 2014. <http://www.afro.who.int/en/clusters-a-programmes/dpc/epidemic-a-pandemic-alert-and-response/outbreak-news/4063-ebola-virus-disease-in-guinea.html> (accessed March 25, 2015).
- 2 WHO. Ebola situation reports. 2015. <http://apps.who.int/ebola/en/current-situation/ebola-situation-report> (accessed March 25, 2015).
- 3 Jones KE, Patel NG, Levy MA, et al. Global trends in emerging infectious diseases. *Nature* 2008; **451**: 990-94.
- 4 Brahmabhatt M, Dutta A. On SARS type economic effects during infectious disease outbreaks. Washington DC: World Bank East Asia and Pacific Region, Chief Economist's Office, 2008.
- 5 Beutels P, Jia N, Zhou Q, Smith R, Cao W, de Vlas S. The economic impact of SARS in Beijing, China. *Trop Med Int Health* 2009; **14**: 85-91.
- 6 World Bank. The economic impact of the 2014 Ebola epidemic: short and medium term estimates for West Africa. Washington, DC: World Bank Group, 2014.
- 7 Pike J, Bogich TL, Elwood S, Finnoff DC, Daszak P. Economic optimization of a global strategy to reduce the pandemic threat. *Proc Natl Acad Sci USA* 2014; **111**: 18519-23.
- 8 Morse SS, Mazet JAK, Woolhouse M, et al. Prediction and prevention of the next pandemic zoonosis. *Lancet* 2012; **380**: 1956-65.
- 9 Janes CR, Corbett KK, Jones JH, Trostle J. Emerging infectious diseases: the role of social sciences. *Lancet* 2012; **380**: 1884-86.
- 10 Mari Saéz A, Weiss S, Nowak K, et al. Investigating the zoonotic origin of the West African Ebola epidemic. *EMBO Mol Med* 2015; **7**: 17-23.
- 11 Karesh WB. Implementing urgent measures for the surveillance and protection of Great Apes in northern Congo in response to recent Ebola outbreaks: final report to U.S. Fish & Wildlife Service on grant number 98210-5-G195. New York, NY: Wildlife Conservation Society, 2007.
- 12 Perrings C, Williamson M, Barbier EB, et al. Biological invasion risks and the public good: an economic perspective. *Conservation Ecology* 2002; **6**.
- 13 Sandler T. Global collective action. Cambridge: Cambridge University Press, 2004.
- 14 Perrings C, Castillo-Chavez C, Chowell G, et al. Merging economics and epidemiology to improve the prediction and management of infectious disease. *Ecohealth* 2014; **11**: 464-75.
- 15 Fenichel E, Castillo-Chavez C, Ceddia M, et al. Adaptive human behavior in epidemiological models. *Proc Natl Acad Sci USA* 2011; **108**: 6306-11.
- 16 Anthony SJ, Epstein JH, Murray KA, et al. A strategy to estimate unknown viral diversity in mammals. *MBio* 2013; **4**: e00598-13.